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PCT

JC14 Rec'd PCT/PTO 27 DEC 2001

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TRANSMITTAL LETTER TO THE UNITED STATES

ATTORNEY'S DOCKET NUMBER 0480/01221DESIGNATED/ELECTED OFFICE (DO/EO/US)  
CONCERNING A FILING UNDER 35 U.S.C. 371

U.S. APPLICATION NO. (If known, see 37 CFR 1.5)

INTERNATIONAL APPLICATION NO.  
PCT/EP00/05848INTERNATIONAL FILING DATE  
23 June 2000PRIORITY DATE CLAIMED  
2 July 1999

TITLE OF INVENTION: SOLID PAROXETINE-CONTAINING PREPARATIONS

APPLICANT(S) FOR DO/EO/US Joerg ROSENBERG, Joerg BREITENBACH, Bernd LIEPOLD

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. /X/ This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.
  2. / / This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.
  3. /X/ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
  4. /x/ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
  5. /X/ A copy of the International Application as filed (35 U.S.C. 371(c)(2)).
    - a. /X/ is transmitted herewith (required only if not transmitted by the International Bureau).
    - b. / / has been transmitted by the International Bureau.
    - c. / / is not required, as the application was filed in the United States Receiving Office (RO/USO).
  6. /X/ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
  7. / / Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)).
    - a. / / are transmitted herewith (required only if not transmitted by the International Bureau).
    - b. / / have been transmitted by the International Bureau.
    - c. / / have not been made; however, the time limit for making such amendments has NOT expired.
    - d. / / have not been made and will not be made.
  8. / / A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
  9. / / An oath or declaration of the inventor(s) (35 U.S.C. 171(c)(4)).
  10. / / A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).
- Items 11. to 16. below concern other document(s) or information included:
11. / / An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
  12. / / An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
  13. /X / A FIRST preliminary amendment.  
/ / A SECOND or SUBSEQUENT preliminary amendment.
  14. / / A substitute specification.
  15. / / A change of power of attorney and/or address letter.
  16. /x / Other items or information.  
International Search Report  
International Preliminary Examination Report

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U.S. Appln. No. (If Known) INTERNATIONAL APPLN. NO.  
PCT/EP00/05848ATTORNEY'S DOCKET NO.  
0480/01221

	CALCULATIONS	PTO USE ONLY
17. /X/ The following fees are submitted		
BASIC NATIONAL FEE (37 CFR 1.492(a)(1)-(5)):		
Search Report has been prepared by the		
EPO or JPO.....\$890.00	890.00	
International preliminary examination fee paid to USPTO		
(37 CFR 1.482).....\$710.00		
No international preliminary examination fee paid to		
USPTO (37 CFR 1.482) but international search fee paid		
to USPTO (37 CFR 1.445(a)(2)).....\$740.00		
Neither international preliminary examination fee		
(37 CFR 1.482) nor international search fee		
(37 CFR 1.445(a)(2)) paid to USPTO .....\$ 1,040.00		
International preliminary examination fee paid to		
USPTO (37 CFR 1.482) and all claims satisfied pro		
-visions of PCT Article 33(2)-(4).....\$100.00		
<b>ENTER APPROPRIATE BASIC FEE AMOUNT = \$ 890.00</b>		
Surcharge of \$130.00 for furnishing the oath or declaration		
later than / / 20 / / 30 months from the earliest		
claimed priority date (37 CFR 1.492(e)).		
<u>Claims</u>	<u>Number Filed</u>	<u>Number Extra</u>
Total Claims	6 -20	
Indep. Claims	1 -3	
Multiple dependent claim(s) (if applicable)		
		Rate
		X\$18.
		X\$84.
		+280.
<b>TOTAL OF ABOVE CALCULATION</b>		<b>= 890.</b>
Reduction of 1/2 for filing by small entity, if applicable.		
Verified Small Entity statement must also be filed		
(Note 37 CFR 1.9, 1.27, 1.28).		
<b>SUBTOTAL</b>		<b>= 890.</b>
Processing fee of \$130. for furnishing the English		
translation later than / / 20 / / 30 months from the		
earliest claimed priority date (37 CFR 1.492(f)).		
<b>TOTAL NATIONAL FEE</b>		<b>= 890 .</b>
Fee for recording the enclosed assignment (37 CFR 1.21(h)).		
The assignment must be accompanied by an appropriate cover		
sheet (37 CFR 3.28, 3.31) \$40.00 per property		
<b>TOTAL FEES ENCLOSED</b>		<b>= \$ 890.00</b>
		Amount to be
		refunded: \$
		Charged \$

- a./X/ A check in the amount of \$ 890.00 to cover the above fees is enclosed.
- b./ / Please charge my Deposit Account No. \_\_\_\_\_ in the amount of \$ \_\_\_\_\_ to cover the above fees. A duplicate copy of this sheet is enclosed.
- c./X/ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 11-0345. A duplicate copy of this sheet is enclosed.

**NOTE:** Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:  
KEIL & WEINKAUF  
1101 Connecticut Ave., N.W.  
Washington, D. C. 20036

Herbert B. Keil  
SIGNATURE

Herbert B. Keil  
NAME

Registration No. 18,967

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of	)	
ROSENBERG et al.	)	BOX PCT
	)	
International Application	)	
PCT/EP 00/05848	)	
	)	
Filed: June 23, 2000	)	
	)	

For: SOLID PAROXETINE-CONTAINING PREPARATIONS

PRELIMINARY AMENDMENT

Honorable Commissioner of  
Patents and Trademarks  
Washington, D.C. 20231

Sir:

Prior to examination, kindly amend the above-identified application as follows:

IN THE CLAIMS

Kindly amend the claims as shown on the attached sheets.

## REMARKS

The claims have been amended to eliminate multiple dependency and to place them in better form for U.S. filing. No new matter is included.

A clean copy of the claims is attached.

Favorable action is solicited.

Respectfully submitted,

KEIL &amp; WEINKAUF



Herbert B. Keil

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(202)659-0100

20011227 10:01:00

CLEAN VERSION OF THE AMENDED CLAIMS - 0480/01221

3. A preparation as claimed in claim 1 having an active ingredient release of at least 80% after 30 min.
4. A process for producing a preparation as claimed in claim 1, which comprises the paroxetine or one of its salts and the matrix material being mixed to give a homogeneous melt in an extruder and subsequently being shaped.

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MARKED UP VERSION OF THE AMENDED CLAIMS - 0480/01221

3. A preparation as claimed in claim 1 [either of claims 1 or 2] having an active ingredient release of at least 80% after 30 min.
4. A process for producing a preparation as claimed in claim 1 [any of claims 1 to 3], which comprises the paroxetine or one of its salts and the matrix material being mixed to give a homogeneous melt in an extruder and subsequently being shaped.

**CLAIMS AS FILED - OZ 0480/01221**

1. A solid or semisolid preparation of paroxetine or one of its physiologically acceptable salts in the form of a molecular dispersion of paroxetine in a pharmaceutically acceptable matrix material which comprises a completely synthetic polymer having a glass transition temperature of  $>90^{\circ}\text{C}$ .
2. A preparation as claimed in claim 1, comprising paroxetine hydrochloride.
3. A preparation as claimed in claim 1 having an active ingredient release of at least 80% after 30 min.
4. A process for producing a preparation as claimed in claim 1, which comprises the paroxetine or one of its salts and the matrix material being mixed to give a homogeneous melt in an extruder and subsequently being shaped.
5. A process as claimed in claim 4 for producing a paroxetine hydrochloride preparation, wherein paroxetine is processed with ammonium chloride and the matrix materials to give a homogeneous melt.
6. A process as claimed in claim 5, wherein amorphous paroxetine or one of its physiologically acceptable salts is employed.

(12) NACH DEM VERTRAG ÜBER DIE INTERNATIONALE ZUSAMMENARBEIT AUF DEM GEBIET DES  
PATENTWESENS (PCT) VERÖFFENTLICHTE INTERNATIONALE ANMELDUNG

(19) Weltorganisation für geistiges Eigentum  
Internationales Büro



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PCT

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WO 01/01956 A3

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9/20, 9/48, A61P 25/24, A61K 9/08

D-68199 Mannheim (DE). LIEPOLD, Bernd [DE/DE];  
U1,8, D-68161 Mannheim (DE).

(21) Internationales Aktenzeichen: PCT/EP00/05848

(74) Anwalt: KINZEBACH, Werner; Reitstötter, Kinzebach  
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(22) Internationales Anmeldedatum:

23. Juni 2000 (23.06.2000)

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(84) Bestimmungsstaaten (regional): europäisches Patent (AT,  
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2. Juli 1999 (02.07.1999) DE

Veröffentlicht:

Mit internationalem Recherchenbericht.

(71) Anmelder (für alle Bestimmungsstaaten mit Ausnahme von  
US): KNOLL AKTIENGESellschaft [DE/DE];  
D-67061 Ludwigshafen (DE).

(88) Veröffentlichungsdatum des internationalen  
Recherchenberichts: 12. Juli 2001

(72) Erfinder; und

(75) Erfinder/Anmelder (nur für US): ROSENBERG, Jörg  
[DE/DE]; Bruchstrasse 29, D-67158 Ellerstadt (DE).  
BREITENBACH, Jörg [DE/DE]; Hans-Sachs-Ring 95A,

Zur Erklärung der Zweibuchstaben-Codes, und der anderen  
Abkürzungen wird auf die Erklärungen ("Guidance Notes on  
Codes and Abbreviations") am Anfang jeder regulären Ausgabe  
der PCT-Gazette verwiesen.

(54) Title: SOLID PREPARATIONS CONTAINING PAROXETINE

(54) Bezeichnung: FESTE PAROXETIN ENTHALTENDE ZUBEREITUNGEN

(57) Abstract: The invention relates to solid or semi-solid preparations of paroxetine or one of the physiologically acceptable salts thereof in the form of a molecular-disperse distribution of paroxetine in a pharmaceutically acceptable matrix material.

(57) Zusammenfassung: Die Erfindung betrifft feste oder halbfeste Zubereitungen von Paroxetin oder einem seiner physiologisch akzeptablen Salze in Form einer molekulardispersen Verteilung des Paroxetins in einem pharmazeutisch akzeptablen Matrixmaterial.

WO 01/01956 A3

# Solid paroxetine-containing preparations

The present invention relates to solid or semisolid preparations  
5 of paroxetine or one of its physiologically active salts in the form of a molecular dispersion in a pharmaceutically acceptable matrix material. The invention further relates to a process for producing such preparations.

10 Paroxetine is the generic name for  
(-)-trans-4-(4-fluorophenyl)-3-(3,4-methylenedioxyphenoxy-methyl)piperidine, which is described, for example, in US-A 4 007 196.

Paroxetine belongs to the class of 5-hydroxytryptamine inhibitors  
15 and is used as antidepressant.

Because of its basicity, paroxetine is employed in the form of its acid addition salts for therapeutic use, in particular in the form of the particularly physiologically acceptable  
20 hydrochloride. However, paroxetine hydrochloride anhydrate shows a tendency to polymorphism. Thus, DE-C 196 03 797 describes four polymorphic forms of paroxetine hydrochloride anhydrate. Polymorphic forms are, however, problematical for therapeutic use since different polymorphs may have different solubilities and  
25 consequently differences in the bioavailability.

One possible solution to the polymorphism problem is to prepare the active ingredient in amorphous form. Thus, WO 99/16440 describes the production of amorphous, i.e. noncrystalline,  
30 paroxetine hydrochloride formulations by dissolving in a hydroxyl-containing compound such as ethanol and then removing this compound. Likewise, EP-A 0 810 224 describes the production of amorphous paroxetine hydrochloride by dissolving the active ingredient in water or a lower alcohol and then removing the  
35 solvent, for example by spray drying.

Dispersions, i.e. homogeneous microdisperse phases, of two or more solids, and the special case of "solid solutions" (molecular dispersion systems), and their use in pharmaceutical technology  
40 are generally known (cf. Chiou and Riegelman, J. Pharm. Sci., 60, 1281-1300 (1971)).

WO 99/00131 describes the production of solid dispersions of substances of low solubility in water using a solvent process or  
45 a melt process. This makes it possible, for example, to produce a solid dispersion of paroxetine hydrochloride in a solid carrier material by melting the free paroxetine base in the presence of



## 2

the carrier material, and then passing dry hydrogen chloride gas through the melt. The melt is then cooled to room temperature, for example by leaving to stand overnight, and is ground.

However, the procedure described in this document is likely to be  
5 confined to the laboratory scale, and is still unsatisfactory in relation to the homogeneity of the mixtures. An additional factor is that the hydrogen chloride gas is very chemically reactive and may react with the excipients and form toxicologically unacceptable products.

10

EP-A 665 009 discloses the possibility of altering the crystalline state of active ingredients by processing in an extruder, the active ingredients being processed essentially without other excipients.

15

In addition, EP-A 760 654 discloses the possibility of producing acid addition salts directly by a melt extrusion process by reacting the free base in the presence of a salt.

20 WO 99/26625 discloses paroxetine formulations in which the active ingredient is dissolved in a copolymer and mixed with a molten polymer. Formulations of this type can also be extruded. However, such formulations are prone to recrystallization, because of the use of a cosolvent.

25

It is an object of the present invention to find improved preparations of paroxetine and its physiologically acceptable salts which, on the one hand, help to avoid the polymorphism problem, but, on the other hand, also have an improved solubility  
30 and storage stability for the active ingredient paroxetine which is of low solubility per se. It was a further object of the invention to provide a simplified process for producing such preparations.

35 We have found that this object is achieved by solid preparations of paroxetine and its physiologically acceptable salts in which the active ingredient is embedded as a molecular dispersion in a pharmaceutically acceptable carrier material which comprises a completely synthetic polymer having a glass transition

40 temperature of  $>90^{\circ}\text{C}$ .

The preparations may also be semisolid, although solid forms are preferred.

45

## 3

Suitable pharmaceutically acceptable salts of paroxetine are not only salts such as, for example, the fumarate or the maleate but also, in particular, the hydrochloride and the corresponding hydrochloride anhydrate.

5

Pharmaceutically acceptable matrix or carrier materials which are suitable in principle are all materials which can be processed by a melt process to give a homogeneous matrix with the active ingredient.

10

Suitable matrix polymers have a glass transition temperature of  $>90^{\circ}\text{C}$ , preferably  $>90$  to  $110^{\circ}\text{C}$ , in the anhydrous state and are completely synthetic polymers. Particularly suitable ones are melt-processable water-soluble polymers such as the homo- or

15 copolymers of N-vinylpyrrolidone with Fikentscher K values in the range from 19 to 100.

Preferred matrix materials are polyvinylpyrrolidones or copolymers of N-vinylpyrrolidone and vinyl acetate such as VP/VAc

20 60/40 (copovidone).

It is also possible to add to the matrix conventional pharmaceutical excipients such as bulking agents, release agents, disintegrants, stabilizers, flavor-improvers, antioxidants or

25 colors.

The novel preparations may contain paroxetine or one of its salts in amounts of from 0.1 to 50% by weight, preferably 5 to 30% by weight, based on the total weight of the preparation.

30

The novel preparations are preferably produced by a melt process, in particular by producing and processing the melt using an extruder.

35 Production can take place by initially producing a powdered premix of all the starting materials and introducing it into an extruder. This premix is processed to a homogeneous melt by introducing shear forces and thermal energy and is subsequently shaped. The melt is preferably produced at temperatures in the  
40 range from  $80$  to  $100^{\circ}\text{C}$ , preferably  $80$  to  $150^{\circ}\text{C}$ . It is also possible initially to melt only the matrix materials and then to meter the active ingredient in through suitable devices.

The extruder employed is preferably a corotating twin screw  
45 extruder. The homogeneous melt produced in this way can either be extruded through a die or a breaker plate, or else be conveyed through the open extruder head and, in this case, where

appropriate, be conveyed directly as granules through grinding elements disposed in the screw channel. The shaping can also take place by conventional pelletizing techniques, for example by hot cut or cold cut or using compressed air.

5

The shaping of the extruded and still plastic melt can also take place by passing the extrudate between counter-rotating calender rolls with depressions, in which case tablet shapes can be produced directly.

10

The novel preparations are preferably produced in the absence of solvents. However, if the starting materials contain solvents, these can be removed in the extruder by applying a vacuum. It is also possible in this way to remove water of crystallization if still present in the active ingredient employed. Suitable solvents are, for example, volatile organic solvents or water.

15

In a particularly preferred embodiment of the invention, the paroxetine salt is produced by processing the free paroxetine base together with a compound which is suitable for forming an appropriate acid addition salt, and the appropriate matrix materials, by a melt extrusion process in an extruder. Ammonium chloride is preferably employed as salt-forming component to produce the corresponding hydrochloride.

20

Preferred novel preparations have instant release of the active ingredient. Instant release means that the release of active ingredient measured in a paddle apparatus at pH 1.2, 50 rpm and 37°C, is at least 80% after 30 min.

25

The novel solid preparations comprise the active ingredient embedded in the form of a molecular dispersion in a matrix. The matrix behaves like a true solvent, i.e. every active ingredient molecule is surrounded by molecules of the matrix materials. This is visually evident from the transparency of the resulting cooled melts. This state of molecular dispersion in the cooled melt is moreover thermodynamically stable, i.e. no recrystallization processes occur. As a consequence of the molecular dispersion of the active ingredient in the matrix, the preparations show instant and uniform release of active ingredient. The active ingredient is essentially released from the solidified melt after 30 min.

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Examination of the extruded melts by differential scanning calorimetry (DSC) no longer shows any melting signals in the region of the active ingredient melting point. In the case of polymeric matrix materials, only broad polymer glass transition steps are evident.

It is also possible according to the invention to employ amorphous paroxetine or its salts. The amorphous forms dissolve more quickly in the matrix because no lattice energy must be supplied for the melting. This makes processing at lower temperatures possible.

The novel preparations are moreover stable to uptake of moisture, i.e. no recrystallization occurs. This is all the more surprising since extremely hydrophilic polymers are employed. The products also show improved storage stability. Surprisingly, paroxetine can be extruded without decomposition despite the sensitive acetal group. This is all the more surprising since PVP and its copolymers have an acidic pH.

The novel preparations can be obtained in the form of granules and be used as such to fill capsules or be compressed to tablets or, as described above, be calendered directly to tablet form or else be used as semisolid preparations to fill capsules.

#### Examples

Powdered premixes of the following composition were processed, employing in each case anhydrous paroxetine hydrochloride:

#### Example 1

Paroxetine hydrochloride	30% by weight
copovidone	70% by weight
finely dispersed silica	
(1% by weight based on	
active ingredient/polymer)	

The powdered premix was melted and extruded in a twin screw extruder with a screw diameter of 16 mm at a material temperature of 145°C. The resulting slightly yellowish transparent melt remained transparent even after cooling. Even after storing per 9 months at 40°C and at 45% relative humidity, the transparency was retained.

## Example 2

A mixture as in Example 1 was extruded analogously through a round-section die with a diameter of 3 mm. To determine the active ingredient release, the cooled, transparent extrudate was divided into pieces weighing 133 mg (paroxetine hydrochloride content of 40 mg). The release was determined by the USP XXII method in a paddle apparatus at pH 1.2, 50 rpm and 37°C:

10	Time [min]	Active ingredient release [% by weight]
	0	0
	5	19
	10	42
	20	82
15	30	96
	60	99

## Example 3

## Production of tablets

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Biconvex tablets with a diameter of 9 mm and a weight of 200 mg were produced by compressing the starting materials in a conventional tablet press (Fette E2 eccentric press) under a pressure of 6.5 kN. The tablet had the following composition:

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paroxetine hydrochloride extrudate from Ex. 1	38% by weight
microcrystalline cellulose	15% by weight
calcium hydrogen phosphate (anhydrous)	35% by weight
Na croscarmellose	10% by weight
30 highly disperse silica	1% by weight
magnesium stearate	1% by weight

The tablets had completely disintegrated in water at 37°C in 5 min.

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10/019049

JC13 Rec'd PCT/PTO 27 DEC 2001

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We claim:

1. A solid or semisolid preparation of paroxetine or one of its  
5 physiologically acceptable salts in the form of a molecular  
dispersion of paroxetine in a pharmaceutically acceptable  
matrix material which comprises a completely synthetic  
polymer having a glass transition temperature of  $>90^{\circ}\text{C}$ .
- 10 2. A preparation as claimed in claim 1, comprising paroxetine  
hydrochloride.
3. A preparation as claimed in either of claims 1 or 2 having an  
active ingredient release of at least 80% after 30 min.
- 15 4. A process for producing a preparation as claimed in any of  
claims 1 to 3, which comprises the paroxetine or one of its  
salts and the matrix material being mixed to give a  
homogeneous melt in an extruder and subsequently being  
20 shaped.
5. A process as claimed in claim 4 for producing a paroxetine  
hydrochloride preparation, wherein paroxetine is processed  
with ammonium chloride and the matrix materials to give a  
25 homogeneous melt.
6. A process as claimed in claim 5, wherein amorphous paroxetine  
or one of its physiologically acceptable salts is employed.

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## Solid paroxetine-containing preparations

## Abstract

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The present invention relates to solid or semisolid preparations of paroxetine or one of its physiologically acceptable salts in the form of a molecular dispersion of paroxetine in a pharmaceutically acceptable matrix material.

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# Declaration, Power of Attorney

Page 1 of 3  
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We (I), the undersigned inventor(s), hereby declare(s) that:

My residence, post office address and citizenship are as stated below next to my name,

We (I) believe that we are (I am) the original, first, and joint (sole) inventor(s) of the subject matter which is claimed and for which a patent is sought in the invention entitled

## Solid preparations containing paroxetine

the specification of which

☐ is attached hereto.

☒ was filed on December 27, 2001 as

Application Serial No. 10/019,049

and amended on \_\_\_\_\_

☒ was filed as PCT international application

Number PCT/EP/00/05848

on June 23, 2000

and was amended under PCT Article 19

on \_\_\_\_\_ (if applicable).

We (I) hereby state that we (I) have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

We (I) acknowledge the duty to disclose information known to be material to the patentability of this application as defined in Section 1.56 of Title 37 Code of Federal Regulations.

We (I) hereby claim foreign priority benefits under 35 U.S.C. § 119(a)-(d) or §365(b) of any foreign application(s) for patent or inventor's certificate, or §365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or PCT International application having a filing date before that of the application on which priority is claimed. Prior Foreign Application(s)

Application No.	Country	Day/Month/Year	Priority Claimed
19930454.8	Germany	02. July 1999	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No



We (I) hereby claim the benefit under Title 35, United States Codes, § 119(e) of any United States provisional application(s) listed below.

\_\_\_\_\_  
(Application Number)

\_\_\_\_\_  
(Filing Date)

\_\_\_\_\_  
(Application Number)

\_\_\_\_\_  
(Filing Date)

We (I) hereby claim the benefit under 35 U.S.C. § 120 of any United States application(s), or § 365(c) of any PCT International application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of 35 U.S.C. § 112. I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR §1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application.

Application Serial No.

Filing Date

Status (pending, patented,  
abandoned)

_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____

And we (I) hereby appoint **Messrs. HERBERT.B.KEIL**, Registration Number 18,967; and **RUSSEL.E.WEINKAUF** Registration Number 18,495; the address of both being Messrs. Keil & Weinkauff, 1101 Connecticut Ave., N.W. Washington, D.C. 20036 (telephone 202-659-0100), our attorneys, with full power of substitution and revocation, to prosecute this application, to make alterations and amendments therein, to sign the drawings, to receive the patent, and to transact all business in the Patent Office connected therewith.

We (I) declare that all statements made herein of our (my) own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine of imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

100  
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